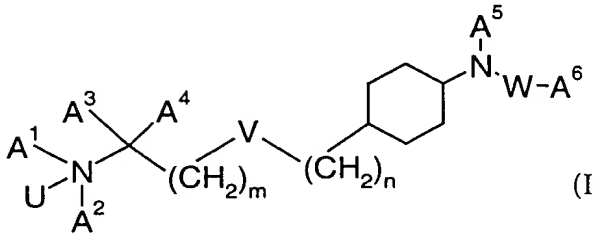
Claims

1. A compound selected from the group consisting of compounds of formula (I)



(I)

wherein

U is O or a lone pair;

V is O, S, $-CH_2-$, -CH=CH-, or $-C\equiv C-$;

W is CO, COO, $CONR^1$, CSO, $CSNR^1$, SO_2, or SO_2NR^1;

m and n are each integers from 0 to 7, with the provisos that m+n is 0 to 7 and m is not 0 when V is O or S;

A^1 is H, lower-alkyl, hydroxy-lower-alkyl, or lower-alkenyl and

A^2 is lower-alkyl, cycloalkyl, cycloalkyl-lower-alkyl, or lower-alkenyl, optionally substituted by R^2, or

A^1 and A^2 bond together to form - A^1- A^2-, wherein - A^1- A^2- is lower-alkylene or lower-alkenylene, optionally substituted by R^2, in which one $-CH_2-$ group of -A^1- A^2- is optionally replaced by NR^3, S, or O;

A^3 and A^4 are each hydrogen or lower-alkyl, or

A^3 and A^4 bond together to form -A^3-A^4-, wherein -A^3-A^4- is $-(CH_2)_{2-5}-$ optionally mono- or multiply-substituted by lower-alkyl;

A^5 is H, lower-alkyl, lower-alkenyl, or aryl-lower-alkyl;

A^6 is lower-alkyl, cycloalkyl, aryl, aryl-lower-alkyl, heteroaryl, heteroaryl-lower-alkyl, lower-alkoxy-carbonyl-lower-alkyl;

R^2 is hydroxy, hydroxy-lower-alkyl, lower-alkoxy, lower-alkoxycarbonyl, $N(R^4,R^5)$, or thio-lower-alkoxy;

R^1, R^3, R^4 and R^5 independently from each other are hydrogen or lower-alkyl; and

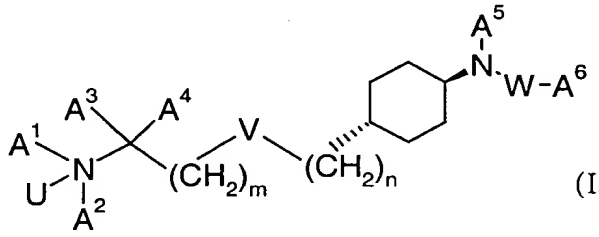
when A^1 is not bonded to A^2 and A^3 is not bonded to A^4, A^1 and A^3 optionally bond together to form -A^1-A^3-, wherein -A^1-A^3- is lower-alkylene or lower-alkenylene, optionally substituted by R^2, in which one $-CH_2-$ group of -A^1-A^3- is optionally replaced by NR^3, S, or O;

pharmaceutically acceptable salts of the compounds of formula (I), and

pharmaceutically acceptable esters of the compounds of formula(I).

2. The compound according to claim 1, wherein A^3 and A^4 are not bonded together.

3. The compound according to claim 1, selected from the group consisting of compounds of formula (Ia)



(Ia)

wherein U, V, W, m, n, A^1, A^2, A^3, A^4, A^5 and A^6 are as defined in claim 1;

pharmaceutically acceptable salts of the compounds of formula (Ia); and

pharmaceutically acceptable esters of the compounds of formula (Ia).

4. The compound according to claim 1, wherein U is a lone pair.

5. The compound according to claim 4, wherein V is O.

6. The compound according to claim 4, wherein V is-CH_2-.

7. The compound according to claim 4, wherein V is -C=C-.

8. The compound according to claim 4, wherein V is -C≡C-.

9. The compound according to claim 4, wherein W is CO, COO, $CONR^1$, $CSNR^1$, SO_2 or SO_2NR^1 and R^1 is hydrogen.

10. The compound according to claim 9, wherein W is COO or SO_2.

11. The compound according to claim 10, wherein n is 0.

12. The compound according to claim 10, wherein n is 1.

13. The compound according to claim 10, wherein m is 1 to 6.

14. The compound according to claims 10, wherein m is 0 and V is -C=C- or -C≡C-.

15. The compound according to claim 10, wherein A^1 is H, methyl, ethyl, isopropyl, 2-hydroxy-ethyl, or 2-propenyl.

16. The compound according to claim 10, wherein A^2 is lower-alkyl, cycloalkyl-lower-alkyl, or lower-alkenyl, optionally substituted with R^2, wherein R^2 is hydroxy, methoxy, or ethoxycarbonyl.

17. The compound according to claim 16, wherein A^2 is methyl, ethyl, 2-hydroxy-ethyl, 2-propenyl, propyl or isopropyl.

18. The compound according to claim 10, wherein A^1 and A^2 are bonded together.

19. The compound according to claim 18, wherein $-A^1-A^2-$ is lower-alkylene or lower-alkenylene, optionally substituted by R^2, in which one $-CH_2-$ group of $-A^1-A^2-$ can optionally be replaced by O, wherein R^2 is hydroxy or 2-hydroxyethyl.

20. The compound according to claim 19, wherein $-A^1-A^2-$ is $-(CH_2)_5-$.

21. The compound according to claim 10, wherein A^3 is hydrogen.

22. The compound according to claim 10, wherein A^4 is hydrogen.

23. The compound according to claim 10, wherein A^3 and A^4 are bonded together to form $-A^3-A^4-$, and $-A^3-A^4-$ is $-(CH_2)_2-$.

24. The compound according to claim 10, wherein A^5 is H, lower-alkyl, lower-alkenyl, or benzyl optionally substituted with halogen.

25. The compounds according to claim 24, wherein A^5 is methyl or ethyl.

26. The compound according to claim 25, wherein A^6 is lower-alkyl, cycloalkyl, phenyl, naphthyl, phenyl-lower-alkyl, pyridyl, indolyl, indolinyl, thienyl, thienyl-methylene, furyl-methylene, benzodioxyl, chinolyl, isoxazolyl, or imidazolyl, optionally substituted by one or more substituents selected from the group consisting of lower-alkyl, lower-alkoxy, lower-alkylcarbonyl, lower-alkoxycarbonyl, fluorine, chlorine, bromine, CN, CF_3, NO_2, or $N(R^6,R^7)$, wherein R^6 and R^7 independently from each other are hydrogen or lower-alkyl.

27. The compound according to claim 26, wherein A^6 is phenyl optionally substituted by one or more substituents selected from the group consisting of fluorine, chlorine, bromine, and CF_3.

28. The compound according to claim 27, wherein A^6 is 4-chloro-phenyl, 4-bromo-phenyl, or 4-trifluoromethyl-phenyl.

29. The compound according to claim 28, wherein A^1 is H, lower alkyl or hydroxy-lower alkyl and A^2 is lower alkyl, hydroxy-lower alkyl or lower alkenyl.

30. The compound according to claim 29, wherein A^3 and A^4 are hydrogen.

31. The compound according to claim 30, wherein V is O.

32. The compound according to claim 30, wherein V is S.

33. The compound according to claim 32, selected from the group consisting of trans-{4-[2-(Allyl-methyl-amino)-ethylsulfanylmethyl]-cyclohexyl}-methyl-carbamic acid 4-

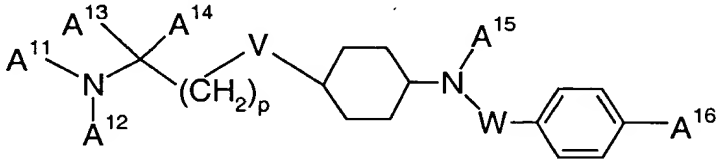
chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

34. The compound according to claim 30, wherein V is-CH_2-.

35. The compound according to claim 30, wherein V is -C=C-.

36. The compound according to claim 30, wherein V is -C≡C-.

37. A compound selected from the group consisting of compounds of formula (Ib)



(Ib)

wherein

V is O, S, -CH_2-, -CH=CH-, or -C≡C-;

W is COO or SO_2;

p is an integer from 0 to 7, with the proviso that p is not 0 when V is O or S;

A^{11} is H, lower-alkyl, or hydroxy-lower-alkyl and

A^{12} is lower-alkyl, hydroxy-lower alkyl, or lower-alkenyl, or

A^{11} and A^{12} bond together to form - A^1- A^2-, wherein - A^1- A^2- is lower-alkylene;

A^{13} and A^{14} are each hydrogen or bond together to form -A^3-A^4-, wherein -A^3-A^4- is -$(CH_2)_{2-5}$-;

A^{15} is lower-alkyl; and

A^{16} is halogen or trifluoromethyl;

pharmaceutically acceptable salts of the compounds of formula (Ib), and

pharmaceutically acceptable esters of the compounds of formula(Ib).

38. The compund according to claim 37, wherein A^{11} is H, lower-alkyl, or hydroxy-lower-alkyl and A^{12} is lower-alkyl, hydroxy-lower alkyl, or lower-alkenyl.

39. The compound according to claim 38, selected from the group consisting of trans-N-{4-[2-(1-dimethylamino-cyclopropyl)-ethoxy]-cyclohexyl}-N-methyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

40. The compound according to claim 37, whereon A^{13} and A^{14} are hydrogen.

41. The compound according to claim 40, selected from the group consisting of trans-4-bromo-N-methyl-N-[4-(2-piperidin-1-yl-ethoxy)-cyclohexyl]-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

42. The compound according to claim 40, selected from the group consisting of trans-methyl-[4-(4-piperidin-1-yl-butyl)-cyclohexyl]-carbamic acid 4-bromo-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

43. The compound according to claim 40, selected from the group consisting of trans-N-methyl-N-[4-(4-piperidin-1-yl-butyl)-cyclohexyl]-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

44. The compound according to claim 40, selected from the group consisting of trans-methyl-[4-(5-piperidin-1-yl-pentyl)-cyclohexyl]-carbamic acid 4-cloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

45. The compound according to claim 40, wherein A^{11} is H, lower-alkyl, or hydroxy-lower-alkyl and A^{12} is lower-alkyl, hydroxy-lower alkyl, or lower-alkenyl.

46. The compound according to claim 45, wherein V is O.

47. The compound according to claim 46, wherein W is COO.

48. The compound according to claim 47, selected from the group consisting of trans-{4-[6-(allyl-methyl-amino)-hexyloxy]-cyclohexyl}-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

49. The compound according to claim 47, selected from the group consisting of trans-{4-[4-(allyl-methyl-amino)-butoxy]-cyclohexyl}-methyl-carbamic acid 4-trifluoromethyl-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

50. The compound according to claim 47, selected from the group consisting of trans-(4-{4-[ethyl-(2-hydroxy-ethyl)-amino]-butoxy}-cyclohexyl)-methyl-carbamic acid 4-trifluoromethyl-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

51. The compound according to claim 47, selected from the group consisting of trans-[4-(4-dimethylamino-butoxy)-cyclohexyl]-methyl-carbamic acid 4-trifluoromethyl-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

52. The compound according to claim 47, selected from the group consisting of trans-{4-[4-(allyl-methyl-amino)-butoxy]-cyclohexyl}-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

53. The compound according to claim 46, wherein W is SO_2.

54. The compound according to claim 53, selected from the group consisting of trans-N-[4-(3-allylamino-propoxy)-cyclohexyl]-N-methyl-4-trifluoromethyl-

benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

55. The compound according to claim 53, selected from the group consisting of trans-N-[4-(6-diethylamino-hexyloxy)-cyclohexyl]-N-methyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

56. The compound according to claim 53, selected from the group consisting of trans-N-[4-(4-dimethylamino-butoxy)-cyclohexyl]-N-ethyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

57. The compound according to claim 53, selected from the group consisting of trans-N-ethyl-N-(4-{4-[(2-hydroxy-ethyl)-methyl-amino]-butoxy}-cyclohexyl)-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

58. The compound according to claim 53, selected from the group consisting of trans-N-(4-{4-[bis-(2-hydroxy-ethyl)-amino]-butoxy}-cyclohexyl)-N-ethyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

59. The compound according to claim 53, selected from the group consisting of trans-4-bromo-N-[4-(2-diisopropylamino-ethoxy)-cyclohexyl]-N-methyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

60. The compound according to claim 45, wherein V is S.

61. The compound according to claim 60, wherein W is COO.

62. The compound according to claim 60, wherein W is SO_2.

63. The compound according to claim 45, wherein V is-CH_2-.

64. The compound according to claim 63, wherein W is COO.

65. The compound according to claim 64, wherein A^{11} is H.

66. The compound according to claim 65, selected from the group consisting of trans-methyl-[4-(5-methylamino-pentyl)-cyclohexyl]-carbamic acid 4-trifluoromethyl-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

67. The compound according to claim 64, wherein A^{11} is methyl.

68. The compound according to claim 67, selected from the group consisting of trans-{4-[5-(allyl-methyl-amino)-pentyl]-cyclohexyl}-methyl-carbamic acid 4-trifluoromethyl-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

69. The compound according to claim 67, selected from the group consisting of trans-{4-[5-(allyl-methyl-amino)-pentyl]-cyclohexyl}-methyl-carbamic acid 4-bromo-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

70. The compound according to claim 67, selected from the group consisting of trans-{4-[5-(allyl-methyl-amino)-pentyl]-cyclohexyl}-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

71. The compound according to claim 67, selected from the group consisting of trans-{4-[4-(allyl-methyl-amino)-butyl]-cyclohexyl}-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

72. The compound according to claim 64, wherein A^{11} is ethyl.

73. The compound according to claim 72, selected from the group consisting of trans-(4-{5-[ethyl-(2-hydroxy-ethyl)-amino]-pentyl}-cyclohexyl)-methyl-carbamic acid 4-trifluoromethyl-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

74. The compound according to claim 72, selected from the group consisting of trans-(4-{5-[ethyl-(2-hydroxy-ethyl)-amino]-pentyl}-cyclohexyl)-methyl-carbamic acid 4-bromo-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

75. The compound according to claim 72, selected from the group consisting of trans-(4-{3-[ethyl-(2-hydroxy-ethyl)-amino]-propyl}-cyclohexyl)-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

76. The compound according to claim 63, wherein W is SO_2.

77. The compound according to claim 76, selected from the group consisting of trans-N-{4-[5-(allyl-methyl-amino)-pentyl]-cyclohexyl}-N-methyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

78. The compound according to claim 76, selected from the group consisting of trans-N-(4-{5-[ethyl-(2-hydroxy-ethyl)-amino]-pentyl}-cyclohexyl)-N-methyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

79. The compound according to claim 45, wherein V is -C=C-.

80. The compound according to claim 79, wherein W is COO.

81. The compound according to claim 79, wherein W is SO_2.

82. The compound according to claim 81, selected from the group consisting of trans-(1E)-N-methyl-N-{4-[3-(methyl-propyl-amino)-propenyl]-cyclohexyl}-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

83. The compound according to claim 81, selected from the group consisting of trans-(1E)-N-(4-{3-[ethyl-(2-hydroxy-ethyl)-amino]-propenyl}-cyclohexyl)-N-methyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

84. The compound according to claim 45, wherein V is -C≡C-.

85. The compound according to claim 84, wherein W is COO.

86. The compound according to claim 85, selected from the group consisting of trans-{4-[3-(allyl-methyl-amino)-prop-1-ynyl]-cyclohexyl}-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

87. The compound according to claim 85, selected from the group consisting of trans-(4-{5-[ethyl-(2-hydroxy-ethyl)-amino]-pent-1-ynyl}-cyclohexyl)-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

88. The compound according to claim 85, selected from the group consisting of trans-methyl-{4-[3-(methyl-propyl-amino)-prop-1-ynyl]-cyclohexyl}-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

89. The compound according to claim 84, wherein W is SO_2.

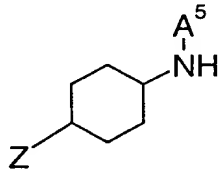
90. The compound according to claim 89, selected from the group consisting of trans-N-[4-(4-dimethylamino-but-1-ynyl)-cyclohexyl]-N-methyl-4-trifluoromethyl-

benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

91. The compound according to claim 89, selected from the group consisting of trans-N-methyl-N-{4-[4-(methyl-propyl-amino)-but-1-ynyl]-cyclohexyl}-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

92. The compound according to claim 89, selected from the group consisting of trans-N-(4-{4-[ethyl-(2-hydroxy-ethyl)-amino]-but-1-ynyl}-cyclohexyl)-N-methyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

93. A process for the manufacture of a compound according to claim 1, comprising reacting a compound of formula (II)



(II)

wherein

A^5 is as defined in claim 1,

Z is a group $(A^1,A^2,)N\text{-}C(A^3,A^4)\text{-}(CH_2)_m\text{-}V\text{-}(CH_2)_n$ or $HO\text{-}(CH_2)_n$, wherein A^1, A^2, A^3,A^4, V, m and n are defined as in claim 1,

with $ClSO_2\text{-}A^6$, $ClCOO\text{-}A^6$, $ClCSO\text{-}A^6$, $OCN\text{-}A^6$, $SCN\text{-}A^6$, $HOOC\text{-}A^6$, or $ClSO_2NR^1\text{-}A^6$, wherein A^6 is as defined in claim 1.

94. A pharmaceutical composition comprising a compound according to claim 1 and at least one of a pharmaceutically acceptable carrier or a pharmaceutically acceptable adjuvant.

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